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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,283	07/18/2003	Robert Stern	UCSF-088CON2	4596

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EXAMINER	
GEBREYESUS, KAGNEW H	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,283	STERN ET AL.	
	Examiner	Art Unit	
	Kagnew H Gebreyesus	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *34-38 and 40-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38 and 40-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 39 is cancelled.

Claims 34-38, 40 and 41 are amended and claims 42-86 are added.

5. Applicant's response to the office action of 08/27/04 is acknowledged. Applicant's arguments filed Feb. 28, 2005 have been fully considered but they have not been found persuasive. Claims 34, 36, 37, 43-47, 49-50, 54-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. These claims are directed to a genus of DNA molecules encoding any hyaluronidase polypeptide from plasma. The specification teaches only a partial structure of a single representative species of a plasma hyaluronidase polypeptide. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of hyaluronidase polypeptide. Furthermore, these claims lack sufficient domain structures identifying pertinent amino acid residues required for glycosylation, fatty acid modifications in addition to residues essential for the active site(s) or a plasma hyaluronidase polypeptide sequence that distinguish it from other hyaluronidase polypeptides.

7. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants traverse the written description rejection on the grounds that the requirement for a claimed genus may be satisfied through sufficient description of a 'representative number of species and that a representative number of species" means that the species which are adequately described are representative of the entire genus. However the claims encompass not only the two plasma hyaluronidases but also any enzyme with or without hyaluronidase activity from any source since the specification defines plasma hyaluronidase as a polypeptide with hyaluronidase activity in addition to any variant with any number of amino acid substitution, addition or deletion. However the teaching in the specification is drawn to a specific plasma hyaluronidase(s).

Regarding original claims 34, 36, 37 and 39 applicants argue that the written description requirement have been complied with by essentially relying on the two sequences (SEQ ID NO: 1 and 3) disclosed in the specification. Applicants disclose that the claimed hpHAses encompasses a hpHAse with substitutions, deletion, addition which encompasses any hyaluronidase as defined in applicant's specification. This definition renders the claims beyond the scope of what has been described since hyaluronidases other than plasma hyaluronidases that exhibit hyaluronidase activity are also encompassed by this definition. Applicant's claims therefore are not limited to the two sequences above or to a specific plasma hyaluronidase(s) as argued in applicant's response. Applicants have not sufficiently described all hyaluronidases from any source. Therefore presently claims 34, 36, 37, 43-47, 49-50, 54-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34-38, 40-58 are rejected under 35 U.S.C. 102(b) as being anticipated by Affify et. al. Affify et. al disclose the purification of hyaluronidase from fresh human serum as starting material to apparent homogeneity in a two-step procedure. This enzyme has an apparent molecular weight of 59 kDa when assayed by SDS-PAGE. Given the similarity of the substrate (hyaluronic acid) used to assay hyaluronidase activity, (described in the materials and methods section of the above reference and the method described by the applicant's specification respectively), the examiner has drawn a correlation between the functional characterization of the native hyaluronidase polypeptide, and structural elements such as glycosylation and fatty acid modification as inherent properties of the native hyaluronidase polypeptide. As such the enzyme inherently meets the limitations of claims 34-38, 40-58.

Applicants declare that the instant invention relates to a highly purified hpHAse and that Affify's purification is a crude preparation. This argument is not agreed to. Affify discloses the purification and characterization of human serum hyaluronidase to apparent homogeneity from fresh human serum as starting material. Furthermore Affify et. al recognize that in the past several enzymatic assays of hyaluronidase activity have failed because of inherent difficulty in either lack of sensitivity or specificity (page 434 second paragraph right column). Affify's enzyme is clearly active and purified to

apparent homogeneity. Furthermore, given that it is isolated from plasma, the proper glycosylation, fatty acid modifications are inherent to the native protein. Therefore the rejection of claims 34-38, 40-58 are maintained under 35 U.S.C. 102(b) as being anticipated by Affify et. al. This enzyme has an apparent molecular weight of 59 kDa when assayed by SDS-PAGE. Claim 40, 42, 52 and 53 are rejected since the specific activity of the hyaluronidase in the reference above (Affify et. al) was defined as the units used to express the activity of the hyaluronidase in the present application is not expressed differs from the units used by Affify's to express the activity of the homogeneous hyaluronidase preparation and that applicants have not provided a declaration regarding the relationship between the units used examiner maintains the rejection under 35 U.S.C. 102(b).

Even if the enzyme preparation disclosed by applicants was purer than that of Affify et. al. the enzyme of Affify et. al is within the broad limitation of claims 34-38, 40-58 since these claims are drawn to a substantially pure enzymatically active enzyme. Claims 55-58 recite degree of homogeneity however the enzyme of Affify et. al is also purified to apparent homogeneity therefore is within the limitations of these claims.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 59-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baumgartner et. al. further in view of Affify et al. Baumgartner et. al. teach the use of a hyaluronidase composition in a phase I trail against chemoresistant Loco-regional Malignant disease. One of ordinary skill in the art would be motivated to use the purified hyaluronidase of Affify et. al for the treatment of malignant disease such as the disease disclosed by Baumgartner et. al. Therefore it would have been obvious to prepare a composition of the protein of Affify et. al together with a pharmaceutical carrier.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the

advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5: 30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kagnew Gebreyesus PhD.

Rebecca Prouty

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